Life

FLEXIBLE STUDIES FOR ONCOLOGY (MULTIPLE CYCLES)

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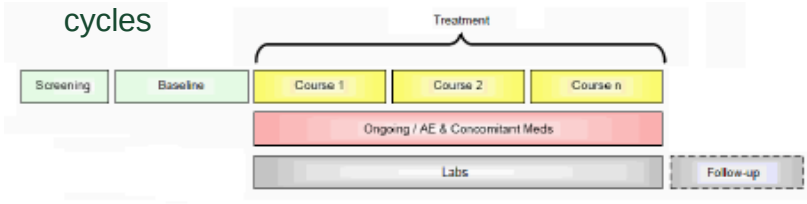
Agenda

- Build flexible studies to manage protocols with multiple cycles and/or multiple arms
- Manage large number of AEs
- Manage List of Tumors on Assessment Forms
- Manage Local Labs

Overview

- In Oncology Studies, there are frequently repeated cycles



- The number of cycles is not always known in advance
- The start of a new cycle may be subject to conditions depending on information recorded at current cycle

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Overview

- AEs are more difficult to handle for Oncology studies, as:
  - ✓ The number of AEs is usually very high
  - ✓ The same AE may occur several times during the study
- Lab data is frequently collected via Local Labs
  - ✓ The OC Lab system does not allow to handle easily Local Lab Assignment
- Some data is usually collected repeatedly, e.g. tumor measurement, and requires multiple entry of the same information
- Unplanned data is frequently collected

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Building Flexible Studies

- ✓ Create Intervals
- ✓ Define DCI Rules & Interval Rules
- ✓ Access to Events and DCIs in RDC
- ✓ Manage unexpected DCIs
- ✓ Calculate & Validate Expectedness of DCIs and Events

Flexible Studies

- Studies in OC may be setup as Flexible in order to allow the creation of interactive DCI Books:
  - ✓ DCIs and intervals may be set to accessible to the User in RDC depending on the Data entered in previous DCIs or intervals
- In order to use this functionality:
  - ✓ The Study must be marked as flexible (before Data Entry started)
  - ✓ The needed Intervals must have been created in OC
  - ✓ DCI Rules and Interval Rules must have been defined in the Enhanced DCI Book

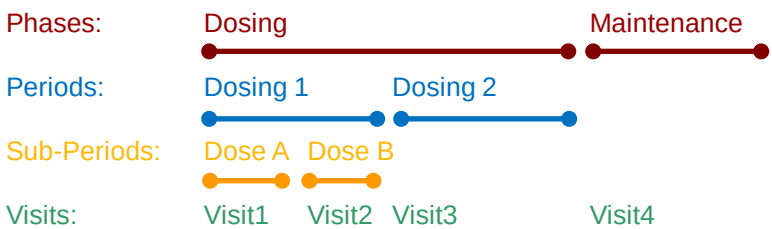
Creating Intervals

- Intervals may be created from the Easy Study Design screen:

- Or from the Intervals menu

Creating Intervals

- Intervals in OC consist of phases that may contain Periods and Sub-Periods:



- Periods and Sub-Periods are optional within OC/RDC but may be useful when setting up Flexible Studies

Creating Intervals

- Periods and Sub-Periods are created from the Phases screen if needed

- All types of Intervals (Phases, Periods and Sub-Periods) may be used to define Interval Rules

Make a Study Flexible

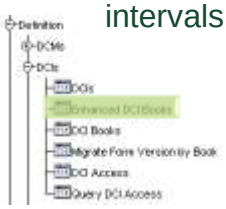
- Studies are made flexible upon creation:

- Or later in the Conduct → Security → Clinical Study States screen:

- This setting cannot be changed once Data Entry already started

Enhanced DCI Book

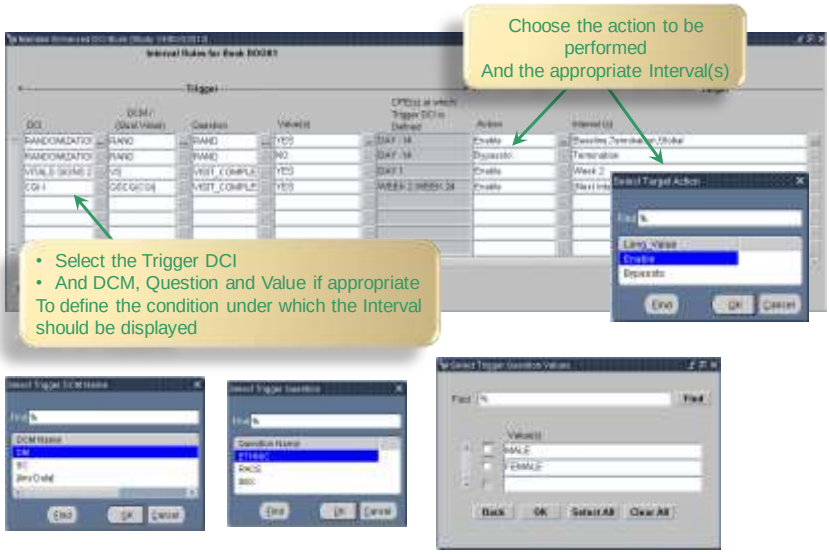
- In flexible studies, Visits and CRFs are displayed dynamically in RDC depending on data previously entered
- The Enhanced DCI Book screen allows DCI Rules and Interval Rules to be defined:
  - ✓DCI rules allow to enable individual DCIs
  - ✓Interval Rules allow to enable one or more intervals



Interval Rules

- Interval Rules are created to:
  - ✓Either enable one or more intervals
  - ✓Or skip one or more intervals
- The Interval Rule can be based
  - ✓Either on presence of any data on a certain DCI (=Trigger DCI)
  - ✓Or the response to a non repeated question having a DVG attached
- Any DCI may be selected as a trigger DCI

Interval Rules



Interval Rules

- Example:
  - ✓ The presence of the “Course Assessment” DCI at a certain Interval enables the next Interval

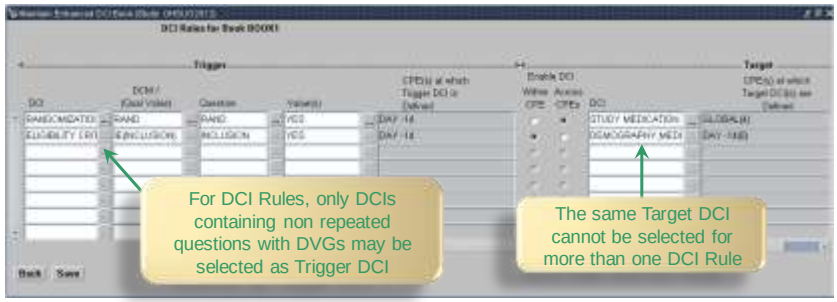
Interval Rules

- Example (cont.):
  - ✓ Define the corresponding Rule in the DCI Book

  - ✓ Note that [any data] means “Any Response”, a DCI marked as blank would not enable the next Interval

DCI Rules

- DCI Rules are created to enable one or more DCIs
  - ✓ Either within a Visit
  - ✓ Or across Visits
- Definition of DCI Rules is similar to definition of Interval Rules



Interval and DCI Rules

- All possible Interval Rules and DCI Rules cannot be defined using enterable questions:
  - ✓ Rules for which the Trigger Question is a numeric value or a Date
  - ✓ Rules based on multiple conditions, e.g.
    - ✦ Enable DCI when Question A=Yes and Question B=No
    - ✦ Enable Next Interval if all mandatory CRFs have been completed
  - ✓ Rules based on DVGs in repeating Question Groups
- In such situations, Derived Questions may be used

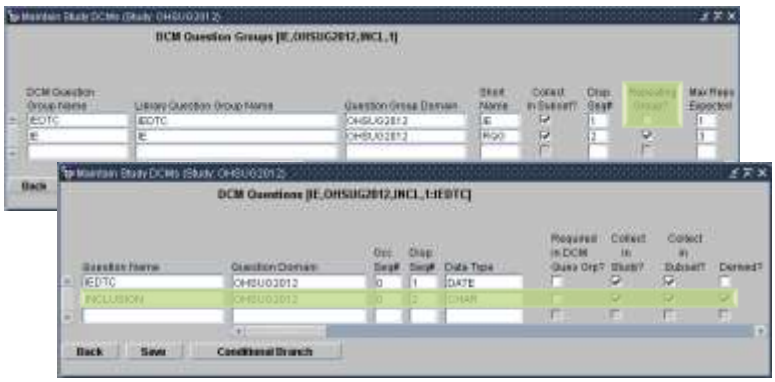
Example of a DCI Rule

- When data for a new Patient is entered:
  - ✓ Initially only the Eligibility and randomization CRFs are displayed:

  - ✓ If all Inclusion Criteria are answered Yes and all Exclusion Criteria are answered No, then all CRFs in the Screening Visit are enabled

Example of a DCI Rule

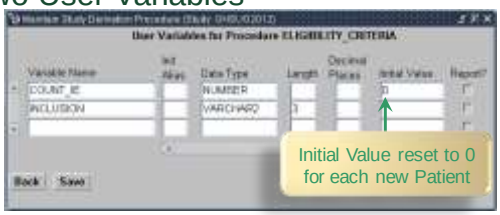
- Include a Derived Question (with a DVG) in the non-repeating Question Group of the Eligibility DCM



Example of a DCI Rule

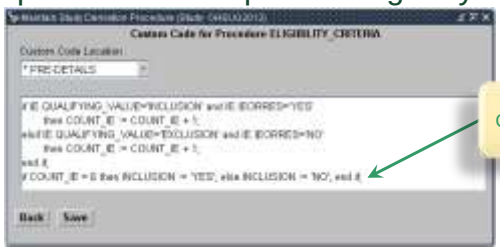
- Create a Derivation Procedure checking whether all Eligibility Criteria are answered as expected

- Include the two Question Groups in the procedure
- Create two User Variables



Example of a DCI Rule

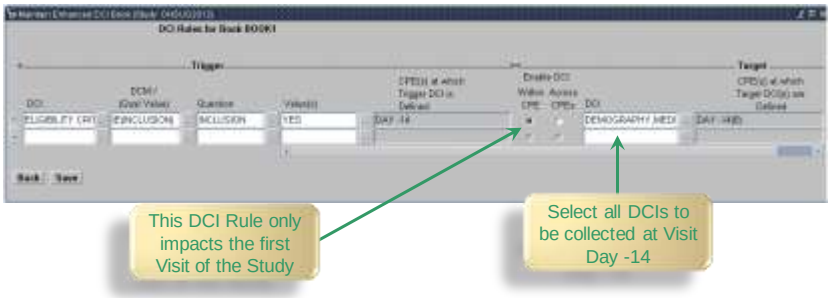
- In the Custom Code, count the number of "correct" responses in the repeated Eligibility Criteria



- At the Detail level, assign the value of the User Variable to the Derived Question

Example of a DCI Rule

- Define the DCI Rule in the DCI Book:
  - ✓ The remaining DCIs should be displayed only when the derived value is set to Yes



Example of a DCI Rule

- All CRFs for the Screening Visit are displayed in case the Eligibility Criteria are entered as expected

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Example of a DCI Rule

- Otherwise only Randomization CRF is available

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Validate the DCI Book

- Once the Enhanced DCI Book is created, and DCI/Interval Rules defined, the DCI Book must be validated

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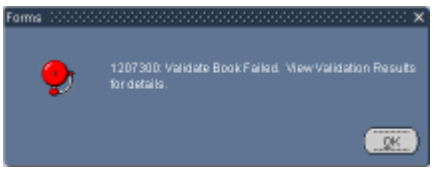
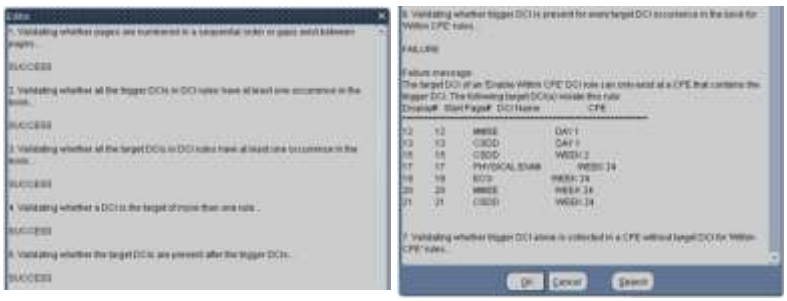
Validate the DCI Book

- If any error is found:
  - ✓A error message is displayed



  - ✓The findings can be reviewed



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Validate the DCI Book

- In case the DCI Book is valid:

- The Validation Status is updated

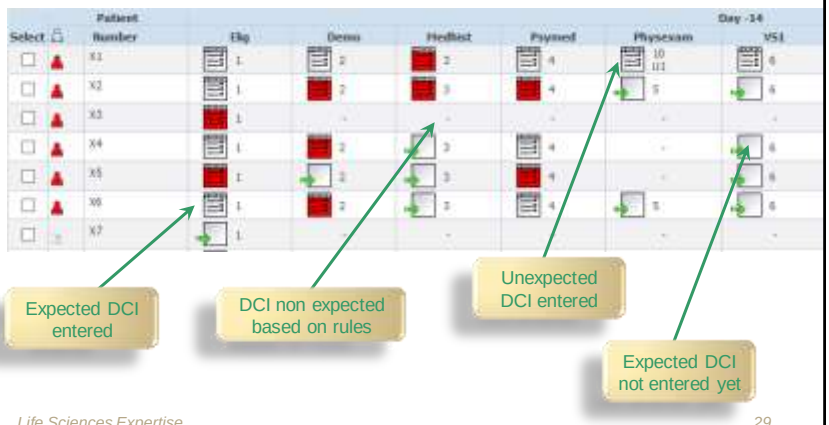
Access to Events in RDC

- Once Interval Rules are defined in OC, only Visits matching these rules are accessible in RDC
- Example:
  - ✓For Patient X1

  - ✓For Patient X3

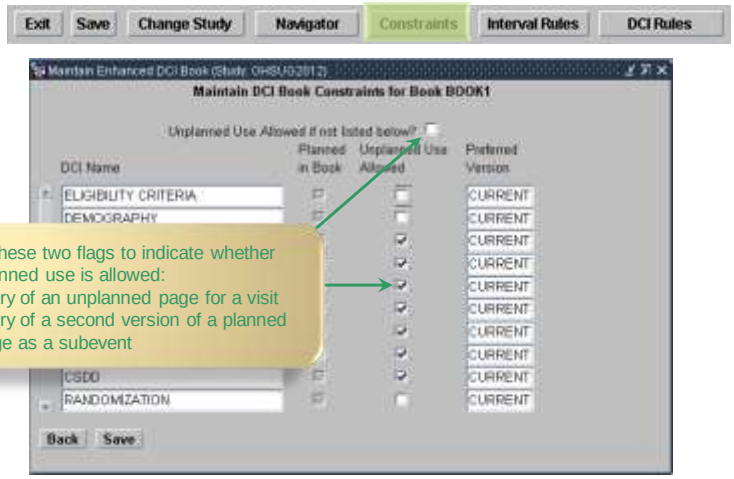
Access to DCIs in RDC

- Once DCIs rules are defined, only DCIs matching the rule are accessible in RDC



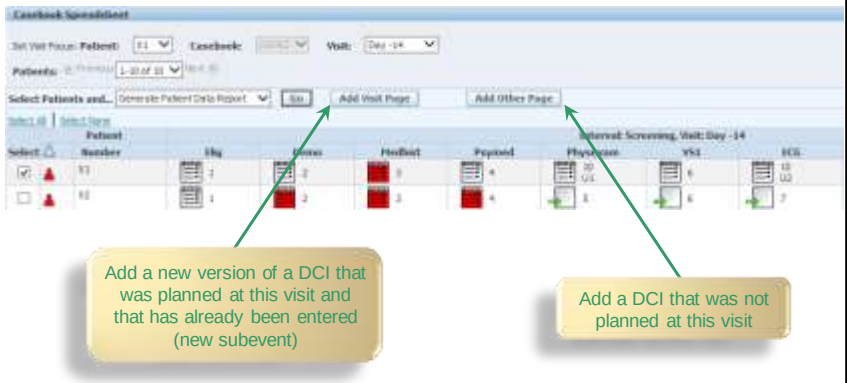
Unexpected DCIs

- Unexpected pages are managed via the DCI Book



Unexpected DCIs

- To add unexpected DCIs in RDC:
  - ✓Select the Patient and
  - ✓Click on “Add Visit Page” or “Add Other Page”



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Calculate Expectedness

- The expectedness of DCIs based on the defined rules is automatically calculated when data is entered or modified
- It is also possible to re-calculate the expectedness of DCIs manually

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Verify Expectedness

- The information related to the DCIs, Visits and Intervals expected for each Patient is stored in the three tables:

Table Name	Description
PP_EXPECTED_INTERVALS	Planned Intervals for each Patient
PP_EXPECTED_CPES	Planned Visits for each Patient
PP_EXPECTED_DCIS	Planned DCIs for each Patient

- Note that:
  - ✓ The corresponding Audit Trail is stored in the tables [*Table Name*]$JN
  - ✓ Equivalent tables exist in Test Mode ([*Table Name*]T)

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Verify Expectedness

- These tracking tables can be used to produce reports verifying which pages or events are expected for a given patient:

PP_EXPECTED_INTERVALS
CLINICAL_STUDY_ID
PATIENT_POSITION_ID
PLAN_INTERVAL_ID
BYPASSED_FLAG

PP_EXPECTED_DCIS
CLINICAL_STUDY_ID
PATIENT_POSITION_ID
CLIN_PLAN_EVE_ID
DCI_ID
CREATION_TS

PP_EXPECTED_CPES
CLINICAL_STUDY_ID
PATIENT_POSITION_ID
CLIN_PLAN_EVE_ID
BYPASSED_FLAG
LAST_EXPECTEDNESS_MOD_TS

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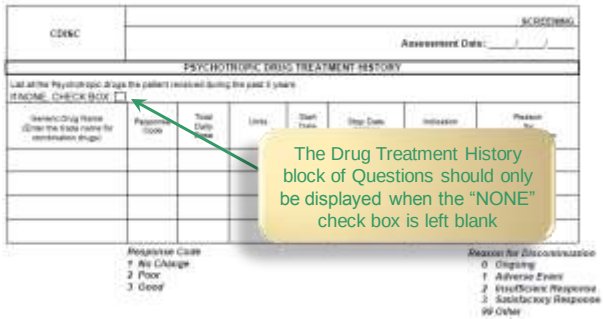
Other flexible features

- ✓ Define conditional Blocks in Data Entry Layouts to restrict data to be collected
- ✓ Display the Interval in addition to the Visit in RDC

Conditional Blocks

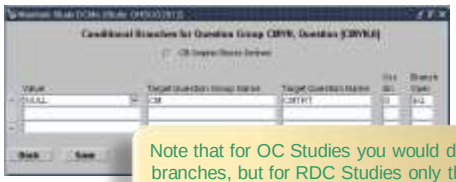
- Conditional Blocks can be setup for Conditional Branches and Indicator Questions in order to display in RDC only the Questions that should be filled in
- Example:



Conditional Blocks

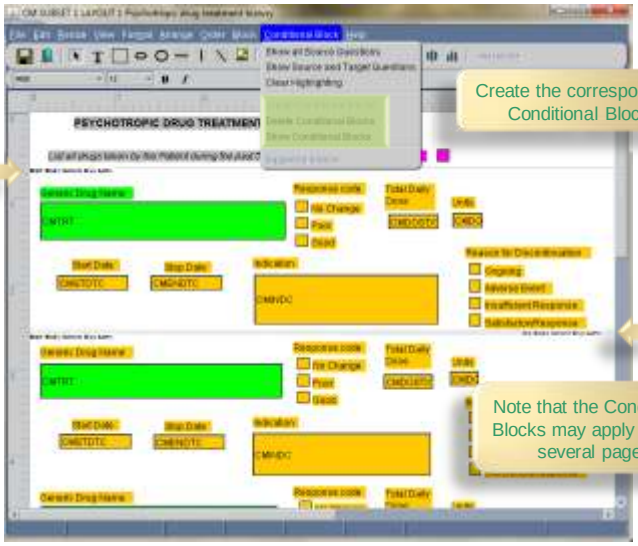
- Define the "None" Question in a non repeating Question Group

- Define the following Conditional Branch



Note that for OC Studies you would define all possible branches, but for RDC Studies only the branch that is not always displayed should be described

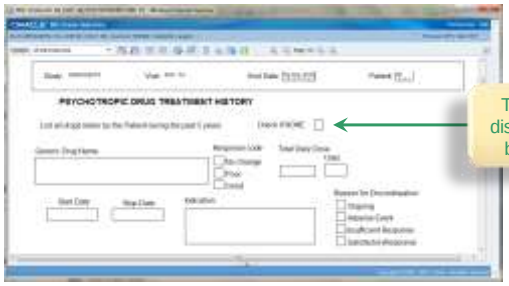
Conditional Blocks

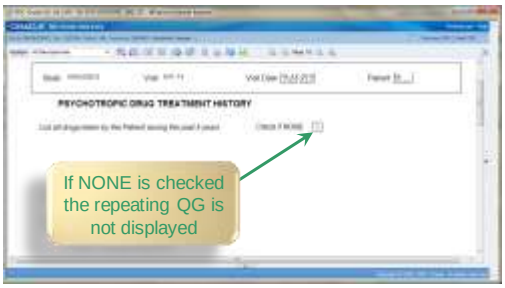


Create the corresponding Conditional Block

Note that the Conditional Blocks may apply across several pages

Conditional Blocks

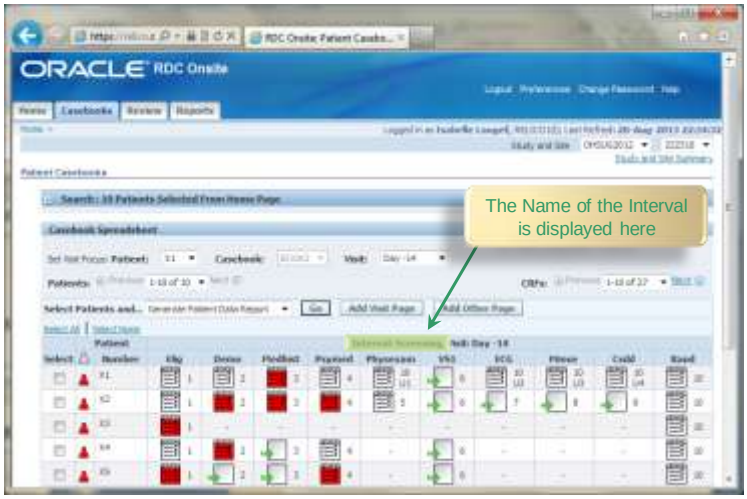




Display the Interval in RDC

- Flexible Studies allow to enable/disable Intervals to match Study Protocols based on multiple courses
  - ✓ However Data Entry is still done at the CPE level and not at the Interval level
- To facilitate the entry of data, the Interval can be displayed in RDC

Display the Interval in RDC



Assign DCI Book to Patients

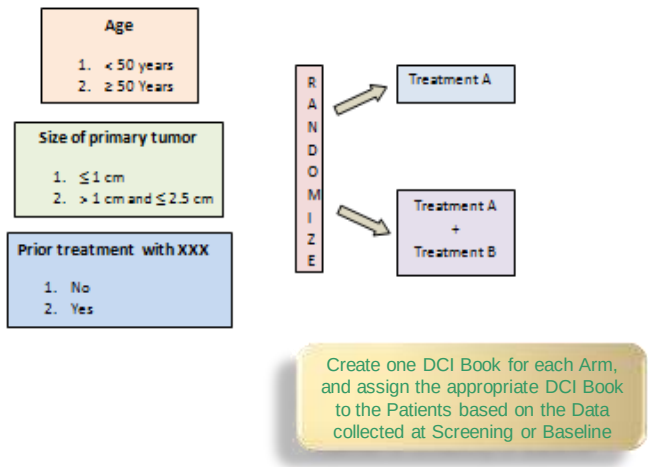
- ✓ A DCI Book must be assigned to each Patient for RDC Data Entry
- ✓ Several DCI Books may be created for complex study Protocols

Studies with multiple Arms

- Designing flexible studies is a way to handle studies with complex protocols
- However depending on the complexity of the DCI and Interval Rules that need to be created, it is sometimes difficult to setup a DCI Book that matches the study Protocol
- It is possible to create multiple DCI-Books in a study and assign the appropriate book to the Patients
  - ✓ Assigning a DCI Book to Patients is required for RDC
  - ✓ This can be done manually, or via a procedure

Studies with multiple Arms

- Example:



Assign a DCI Book to Patients

- The usual way to assign a DCI Book to Patients is to use the Patient Positions screen:
  - ✓ Either enter manually the DCI Book name for each Patient

  - ✓ Or Use the "Assign DCI Book" button

Assign a DCI Book to Patients

- This usual method is not convenient when the DCI Book assigned to the Patients depends on data collected
- In this case it is possible to assign a DCI Book to a Patient using a Validation Procedure

Assign a DCI Book to Patients

- In the Custom Code use the procedure set_patient_book provided by Oracle and apply any needed condition

- Create a User Variable

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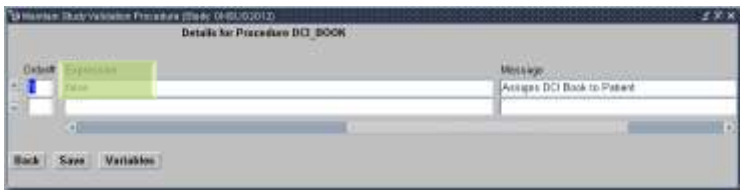
Assign a DCI Book to Patients

- The Detail line of the Validation procedure should not generate any discrepancy:



- Set the Execution Context field to the appropriate value:

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Manage Adverse Events

- ✓ The number of AEs per Patient may be very high
- ✓ This may cause troubles when designing the AE form and when updating existing AEs

Manage AEs

- The first concern regarding Adverse Events is how to setup the forms:
  - ✓ Create one form per AE and one Visit to collect Adverse Event seems the easiest option
    - ✦ However this means that new AEs are created with new subevents, which means the maximum number of AEs per patient is 100
  - ✓ Create one AE form with multiple repeats is a good way to handle data when the number of expected AEs is high
    - ✦ However designing such a layout with many questions and repeats may be difficult during setup and data entry

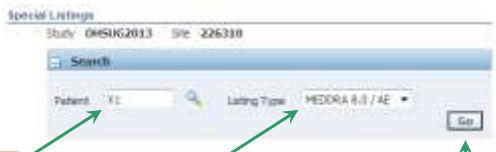
Manage AEs

- The first concern regarding Adverse Events is how to setup the forms (cont.):
  - ✓ Create several AE forms or collect AEs at multiple Visits (for example one visit per cycle) seems a nice setup alternative
    - ✦ However when updating AEs (entry of resolution or followup information) the site user may have troubles to find the correct AE

Manage AEs

- The Special Listing View in RDC allows to review all AEs and retrieve a page that needs to be updated

- Select the Patient and the type of data you want to review:



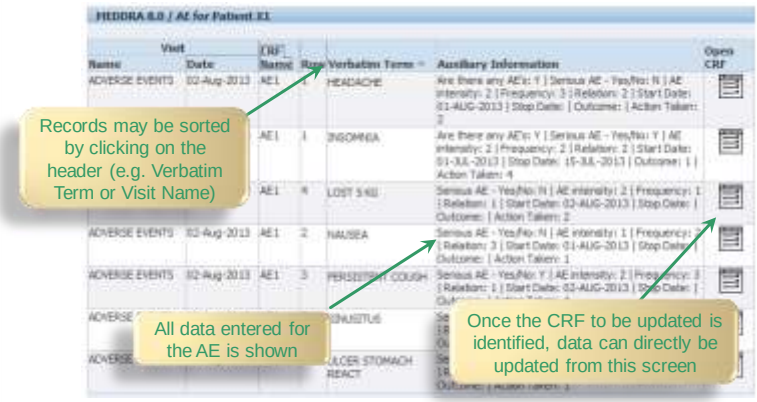
The Special Listing View only displays data for one specific Patient

Any data collected on a page that is coded may be displayed

Click on Go

Manage AEs

- All AEs for the selected Patient are listed:



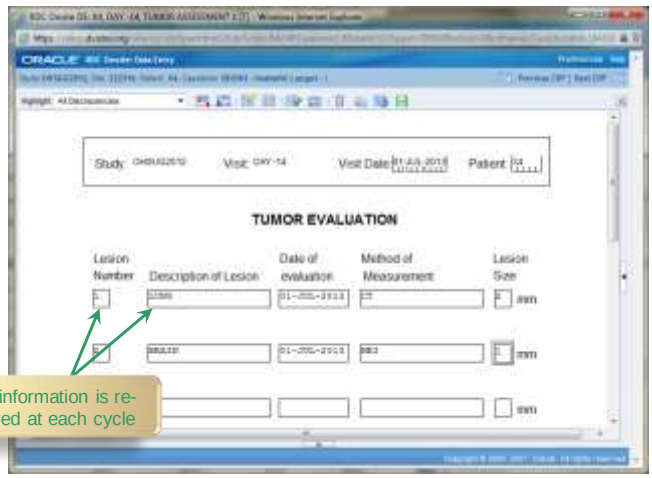
- Alternative solution: Create a new Activity to be displayed on the Home Page

Manage List of Tumors

- ✓ At each cycle there is usually a tumor assessment form listing all tumors previously evaluated
- ✓ This list is usually entered manually, but may be derived (if not batch loaded)

Manage List of Tumors

- The Tumor Assessment CRF usually looks like this:



Manage List of Tumors

- If the data is batch loaded, it is easy to incorporate a preprocessing check verifying that the Lesion Number, Location, and/or Description are consistent across cycles
- However when the data is entered manually, it would be more convenient to be able to enter this list only once and then display automatically the information on further cycles
  - ✓ Default Values cannot be used for that
  - ✓ Create a Thesaurus DVG would not help to ensure that the data is properly entered at each cycle as the data depends on the patient

Manage List of Tumors

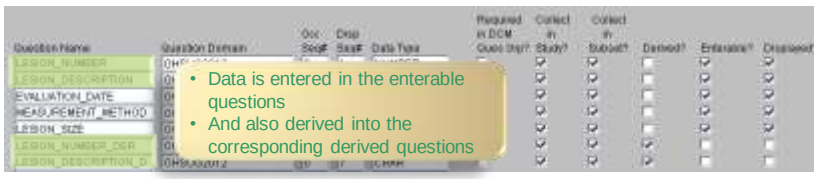
- Create a derivation procedure might help, but:
  - ✓ Either the Site User enters the assessment data without seeing the Lesion Description, as a derivation procedure can only be executed when saving the page
  - ✓ Or the User opens simultaneously a previously completed Tumor Assessment form to view the Lesion details

Manage List of Tumors

- To create such a procedure:
  - ✓ Create two subsets for this DCM

DCM Name	Subset #	Layout #	Name	Domain	Status	Short Name	Type	Description
TUMOR_ASSESSME	1	1	TASS1	OHSUG2012	A	TASS	PHYSICAL EXAM	Tumor Assessment
TUMOR_ASSESSME	2	1	TASS2	OHSUG2012	P	TASS	PHYSICAL EXAM	Tumor Assessment

  - ✓ Subset 1 is used to collect the initial data:



  - ✓ Subset 2 does not use at all the two enterable questions

Manage List of Tumors

- When creating the procedure:
  - ✓ Set the Execution Context to “ON-LINE/DCM”:

  - ✓ Include the Question Group twice (once for the initial data and once for the new data):

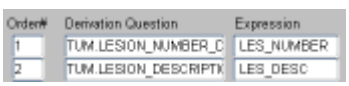
  - ✓ Include the 4 Questions in each Procedure QG:

Manage List of Tumors

- When creating the procedure (cont.):
  - ✓ You need to create two User Variables:

  - ✓ Assign a value to the User Variables in the Custom Code:

  - ✓ And define the Details:



Manage List of Tumors

- Once the Site User enters new Tumor Assessment data and saves the page

- The Lesion information previously entered is automatically populated:

Manage Local Labs

- ✓ Lab data is frequently collected via Local Labs
- ✓ Assigning the correct Lab when having a long list of Labs is a difficult task particularly if done in RDC

Manage Local Labs

- The management of Local Labs may be facilitated by using Thesaurus DVGs and restricting the values displayed to the current study and site
  - ✓ Define a Thesaurus DVG Listing Labs by address and link Labs to Sites by location (e.g. country, state..)
  - ✓ Add a Question in the Lab DCM having this Thesaurus DVG assigned
  - ✓ The Site User will see only the list of Local Labs (or enter a new Lab name)
  - ✓ Then derive the selected Lab Name (if found in the DVG) to the Lab field in the DCM Header

Manage Local Labs

- Example:
  - ✓ You first need to create a view:

In this example, "Local" means "in the same country"!

  - ✓ And define the matching Thesaurus DVG in OC:

Manage Local Labs

- Example (cont.):
  - ✓ In RDC, the Site User can select a Lab from the List:

  - ✓ A Discrepancy is created when another Lab is entered manually

Manage Local Labs

- To fill-in properly the Lab field in the DCM Header:
  - ✓ You need to use a **Validation** Procedure
  - ✓ Enter the SQL code populating the Lab field based on the entry of the Site User in the Custom Code
  - ✓ Leave the Lab field blank in case a Thesaurus DVG was created upon Data Entry
  - ✓ Create a Detail that does not produce any discrepancy (e.g. Expression = false)

Life Sciences Expertise

Questions?

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Biography

- Isabelle Laugel has a background of mathematician and software developer specialized in security of computer systems and optimization
- She is working in the pharmaceutical industry since 15 years and provides training, validation, consulting and support services for Life Sciences applications and business processes to pharmaceutical companies, medical devices companies and CROs of any size worldwide
- She founded Life Sciences Expertise in 2011 in order to share her experience in Data Management and Drug Safety